

# PATENT COOPERATION TREATY

PART of # B  
10/028392

From the INTERNATIONAL SEARCHING AUTHORITY

**RECEIVED**

**PCT**

To:  
BRISTOL-MYERS SQUIBB COMPANY  
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UNITED STATES OF AMERICA

**BMS PATENT LAW**

INVITATION TO PAY ADDITIONAL FEES

DEC 18 2002

(PCT Article 17(3)(a) and Rule 40.1)

**Docketed Item**

**Due Date**

**Attorney**

Date of mailing  
(day/month/year)

06/12/2002

Applicant's or agent's file reference

D0085 PCT

**PAYMENT DUE**

within **45** ~~days~~ days  
from the above date of mailing

International application No.

PCT/US 01/ 50457

International filing date  
(day/month/year)

20/12/2001

Applicant

BRISTOL-MYERS SQUIBB COMPANY

**1. This International Searching Authority**

- (i) considers that there are 2 (number of) inventions claimed in the international application covered by the claims indicated ~~below~~ on the extra sheet:

and it considers that the international application does not comply with the requirements of unity of invention (Rules 13.1, 13.2 and 13.3) for the reasons indicated ~~below~~ on the extra sheet:

- (ii) ☒ has carried out a partial international search (see Annex) ☐ will establish the international search report on those parts of the international application which relate to the invention first mentioned in claims Nos.:

**1-23 partly**

- (iii) will establish the international search report on the other parts of the international application only if, and to the extent to which, additional fees are paid

**2. The applicant is hereby invited, within the time limit indicated above, to pay the amount indicated below:**

EUR 945,00 x 1 = EUR 945,00  
Fee per additional invention      number of additional inventions      total amount of additional fees

Or, \_\_\_\_\_ x \_\_\_\_\_ = \_\_\_\_\_

The applicant is informed that, according to Rule 40.2(c), the payment of any additional fee may be made under protest, i.e., a reasoned statement to the effect that the international application complies with the requirement of unity of invention or that the amount of the required additional fee is excessive.

3. ☒ Claim(s) Nos. further info have been found to be unsearchable under Article 17(2)(b) because of defects under Article 17(2)(a) and therefore have not been included with any invention.

Name and mailing address of the International Searching Authority



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Authorized officer

Henriëtte Huysing-Solles

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-23 partly

Polypeptides with amino acid sequence with seq.id.2  
and corresponding nucleotide sequence with seq.id.1 ,  
corresponding recombinant vector , antibodies, host cell,  
method of making a polypeptide or polynucleotide .

2. Claims: 1-23 partly

Polypeptides with amino acid sequence with seq.id.35  
and corresponding nucleotide sequence with seq.id.34  
corresponding recombinant vector , antibodies, host cell,  
method of making a polypeptide or polynucleotide .

TANIGUCHI H. et al. MOLECULAR BRAIN RESEARCH, ELSEVIER SCIENCE BV, AMSTERDAM, NL, VOL - 36 , NR - 1, PG - 45-52, 1996 , disclose the cloning and expression of a gene for a protein with leucine-rich repeats LR in the developing mouse nervous system . This protein NLRR-3 has LRRs with amino- and carboxy-terminal LRR-flanking regions which are conserved among adhesive proteins and signal-transducing receptors in this family .

(see the abstract and figs.3,4)

The corresponding TREMBLREL with accession number P97860 discloses that its sequence contains the following domains sm00408, IGc2, Immunoglobulin C-2 Type ; pf00047, ig, Immunoglobulin domain ; pf01463, LRRCT, Leucine rich repeat C-terminal domain ; sm00082, LRRCT, Leucine rich repeat C-terminal domain ; sm00013, LRRNT, Leucine rich repeat N-terminal domain ; sm00369, LRR\_TYP, Leucine-rich repeats (see the RT and DR fields )

TREMBLREL with accession number P70193 discloses the protein LIG-1 with leucine-rich repeats from glial cells in the mouse brain , having the following domains Pfam PF00047 ig ; Pfam PF014 63 LRRCT ; SMART SM00408 IGc2 ; SMART SM00082 LRRCT ; SMART SM00013 LRRNT; and SMART SM00369 LRR\_TYP;

(see the RT and DR fields)

TREMBLREL with accession number 094898 discloses the human protein KIAA0806 from cDNA clones from brain , having the following domains Pfam PF00047 ig; Pfam PF00560 LRR ; Pfam PF01463 LRRCT; SMART SM00408 IGc2 ; SMART SM00082 LRRCT; SMART SM00013 LRRNT ; and SMART SM00369 LRR\_TYP .

(see the RT,DE and DR fields)

TREMBLREL with accession number Q92626 discloses the human protein KIAA0230 fragment from cDNA clones from cell line KG-1 and brain , having the following domains Pfam PF00047 ig ; Pfam PF00560 LRR ; Pfam PF01463 LRRCT ; SMART SM00408 IGc2 ; SMART SM00082 LRRCT ; SMART SM00013 LRRNT and SMART SM00369 LRR\_TYP .

(see the RT,DE and DR fields)

In view of the prior art, the problem of underlying application can be defined as providing further nervous system protein with leucine-rich repeats .

The 1st solution to the problem is the provision of leucine-rich repeats containing polypeptides with amino acid sequence with seq.id.2 and corresponding nucleotide sequence with seq.id.1 .

The 2nd solution to the problem is the provision of leucine-rich repeats containing polypeptides with amino acid sequence with seq.id.35 and corresponding nucleotide sequence with seq.id.34 .

In view of the fact that mouse and human nervous system protein with leucine-rich repeats have been disclosed in the prior-art , comprising different leucine repeat domains and IG domains , due to the essential differences in structure containing different leucine repeats of the two solutions , due to the fact that no other technical features can be distinguished which, in the light of the prior art, could be regarded as special technical features, the international searching authority is of the opinion that there is no single inventive concept underlying the plurality of the present application

in the sense of Rule 13.1 PCT .

Consequently there is a lack of unity and the different inventions , not belonging to a common inventive concept , are formulated as the different subjects in the communication pursuant to Article 17(3) (a) PCT.

Therefore, and bearing in mind that every one of the two inventions distinguished above requires a separate search in the appropriate databases and classified documentation , the International Search Authority considers that the PCT guidelines VII, 12 regarding complete search with negligible additional work is not applicable . Thus only the first invention ( claims 1-23 partly , see above ) has been fully searched .

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 206

Continuation of Box 3.

Although claims 11,21,23 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition. Although claims 12,13 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

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1. The present communication is an Annex to the invitation to pay additional fees (Form PCT/ISA/206). It shows the results of the international search established on the parts of the international application which relate to the invention first mentioned in claims Nos.:

**1-23**

2. This communication is not the international search report which will be established according to Article 18 and Rule 43.

3. If the applicant does not pay any additional search fees, the information appearing in this communication will be considered as the result of the international search and will be included as such in the international search report.

4. If the applicant pays additional fees, the international search report will contain both the information appearing in this communication and the results of the international search on other parts of the international application for which such fees will have been paid.

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TANIGUCHI H ET AL: "CLONING AND EXPRESSION OF A NOVEL GENE FOR A PROTEIN WITH LEUCINE- RICH REPEATS IN THE DEVELOPING MOUSE NERVOUS SYSTEM" MOLECULAR BRAIN RESEARCH, ELSEVIER SCIENCE BV, AMSTERDAM, NL, vol. 36, no. 1, 1996, pages 45-52, XP000865556 ISSN: 0169-328X abstract; figures 1-4 ---	1-10, 14-20
X	DATABASE TREMBLREL 'Online! 1 May 1997 (1997-05-01) TANIGUCHI H. ET AL.: "Leucine-rich repeat protein precursor (Fragment)" retrieved from EBI Database accession no. P97860 XP002221308 the whole document ---	1-10, 14-20
X	DATABASE TREMBLREL 'Online! 1 February 1997 (1997-02-01) SUZUKI Y. ET AL.: "Membrane glycoprotein LRIG1 OR IMG" retrieved from EBI Database accession no. P70193 XP002221309 the whole document ---	1-10, 14-20

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Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

\* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

**Annex to Form PCT/ISA/206  
COMMUNICATION RELATING TO THE RESULTS  
OF THE PARTIAL INTERNATIONAL SEARCH**

International Application No  
**PCT/US 01/50457**

**C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT**

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE TREMBLREL 'Online! 1 May 1999 (1999-05-01) NAGASE T. ET AL.: "Hypothetical protein KIAA0806" retrieved from EBI Database accession no. 094898 XP002221310 the whole document</p> <p align="center">---</p>	1-10, 14-20
X	<p>DATABASE TREMBLREL 'Online! 1 February 1997 (1997-02-01) NAGASE T. ET AL.: " MYELOBLAST KIAA0230 (Fragment)" retrieved from EBI Database accession no. Q92626 XP002221311 the whole document</p> <p align="center">---</p>	1-10, 14-20
X	<p>DATABASE TREMBLREL 'Online! BLUM, H. ET AL.: " Hypothetical protein (Fragment)." retrieved from EBI Database accession no. Q9NT99 XP002221312 the whole document</p> <p align="center">---</p>	1-10, 14-20
X	<p>DATABASE EMBL 'Online! 4 August 1999 (1999-08-04) " Homo sapiens chromosome 19 clone CTD-2560K21, complete sequence." retrieved from EBI Database accession no. AC008743 XP002221313 the whole document</p> <p align="center">---</p>	1-10, 14-20
A	<p>WO 99 20644 A (GENETICS INST) 29 April 1999 (1999-04-29) page 109 -page 111; claim 26</p> <p align="center">-----</p>	1-10, 14-20

# Patent Family Annex

Information on patent family members

International Application No

PCT/US 01/50457

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9920644	A	29-04-1999	AU 1101199 A 10-05-1999
			CA 2306457 A1 29-04-1999
			EP 1037899 A1 27-09-2000
			JP 2001520033 T 30-10-2001
			WO 9920644 A1 29-04-1999